For the treatment of postmenopausal women with osteoporosis at high risk for fracture

Her 12th dose of EVENITY® is here

Plan her transition to Prolia®

Transition her to Prolia® 1 month * after completing EVENITY® to build on her BMD progress [1,2]

*In the FRAME study, Prolia® was initiated 1 month +/- 7 days from the last monthly dose of EVENITY®.

EVENITY® (romosozumab-aqqg) injection 105 mg/1.17 mL

prolia® (denosumab) injection

INDICATION

EVENITY® is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

The anabolic effect of EVENITY® wanes after 12 monthly doses of therapy. Therefore, the duration of EVENITY® use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an antiresorptive agent should be considered.

IMPORTANT SAFETY INFORMATION

POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH

EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY® should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENITY® should be discontinued.

Please see additional EVENITY® Important Safety Information on page 8.

INDICATION

Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

Prolia® is contraindicated in patients with hypocalcemia, women who are pregnant, and patients with a history of systemic hypersensitivity to any component of the product. Perform pregnancy testing in women of reproductive potential prior to initiating treatment with Prolia®.

Please see additional Prolia® Important Safety Information on pages 10 and 11.

BMD = bone mineral density.

Plan her next steps with Prolia®

The 12th monthly dose is an important milestone for your EVENITY® patients. EVENITY® is proven to rapidly build bone in just 12 monthly doses. She needs a plan that will help build on her progress following EVENITY®. [1]

Osteoporosis is a chronic and progressive disease that requires ongoing management. [3] Without a follow-up therapy, her BMD may decline and her fracture risk may rise. [1,4]

Help keep her on track by taking action at 12 months.

At her 12th monthly dose of EVENITY®, talk to your patient about transitioning to Prolia®

*In the FRAME study, Prolia® was initiated 1 month +/- 7 days from the last monthly dose of EVENITY®.

Important Safety Information for Prolia®

Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue Prolia®.

Please see additional Prolia® Important Safety Information on pages 10 and 11.

Consider a DXA scan to evaluate her BMD results following EVENITY®

Commonly asked questions about a DXA after 12 monthly doses

Q **How often is a DXA covered for my EVENITY® patients?**

A For patients completing EVENITY® treatment, measuring results with a DXA after 12 monthly doses may be covered by Medicare when medically necessary. [1,5,6]

Q **How do I know if my EVENITY® patients will qualify for a covered DXA?**

A If you are monitoring your patient to assess osteoporosis therapy, this assessment qualifies as a covered bone mass measurement (BMM) under Medicare Part B. [5]

Q **Which CPT® code could I use to have my patient's DXA covered?**

A There is no deductible or coinsurance for your patients when you use BMM code CPT® 77085 (this aligns with other DXA-related codes). [7]

CPT® = current procedural terminology; DXA = dual-energy x-ray absorptiometry.

Codes are provided here for reference purpose only. The responsibility to determine coverage and reimbursement parameters, and appropriate coding for a particular patient and/or procedure, is always the responsibility of the provider or physician.

AACE and NOF clinical guidelines support ongoing monitoring to assess treatment progress [8,9]

AACE = American Association of Clinical Endocrinologists; NOF = National Osteoporosis Foundation.

Important Safety Information for EVENITY®

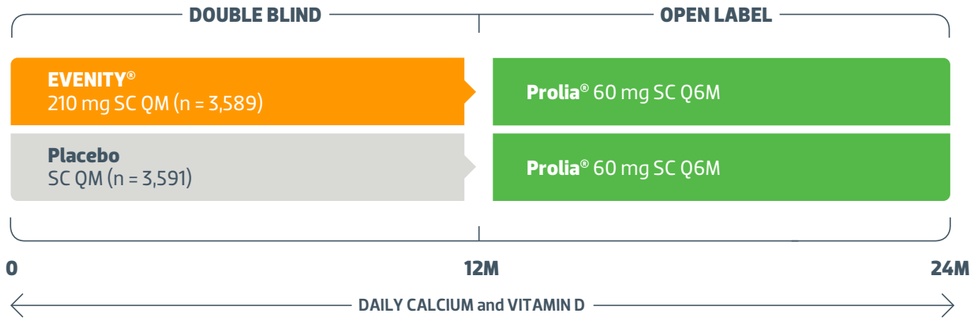
EVENITY® is contraindicated in patients with hypocalcemia, and patients with a history of systemic hypersensitivity to romosozumab or to any component of the product formulation.

Please see additional EVENITY® Important Safety Information on page 8.

The EVENITY® to Prolia® sequence was evaluated in a study of over 7,000 women with postmenopausal osteoporosis

A randomized, double-blind pivotal trial with co-primary endpoints of new vertebral fracture at month 12 and 24

Phase 3 study in postmenopausal women with osteoporosis receiving EVENITY® first followed by Prolia® vs placebo followed by Prolia® [10]



SC = subcutaneous; QM = monthly; Q6M = every 6 months.

Study design: A randomized, double-blind, placebo-controlled study of postmenopausal women aged 55 to 90 years with BMD T-score ≤ –2.5 at the total hip or femoral neck. 7,180 women were randomized to receive subcutaneous injections of either EVENITY® (n = 3,589) or placebo (n = 3,591) for 12 months. After the 12-month treatment period, women in both arms transitioned to open-label antiresorptive therapy (denosumab) for 12 months while remaining blinded to their initial treatment. All women were supplemented with daily calcium and vitamin D [1]
Co-primary endpoints: New vertebral fracture at month 12 and month 24 [1]
Secondary endpoints: Cumulative incidence of clinical (nonvertebral and symptomatic vertebral), nonvertebral, and other fractures at 12 and 24 months [10,*]
Additional endpoints: Change from baseline in BMD at lumbar spine, total hip, and femoral neck at 12 and 24 months [10]
Mean age: 71 years [1]
Fracture history: 18.3% with prevalent vertebral fracture [†], 21.7% with previous nonvertebral fracture [10]

*Other fractures: major nonvertebral fracture, new or worsening vertebral fracture, hip fracture, major osteoporotic fracture, and multiple new or worsening vertebral fractures.
[†]Majority of which were mild in severity.

EVENITY® (romosozumab-aqqg) injection 105 mg/1.17 mL | prolia® (denosumab) injection

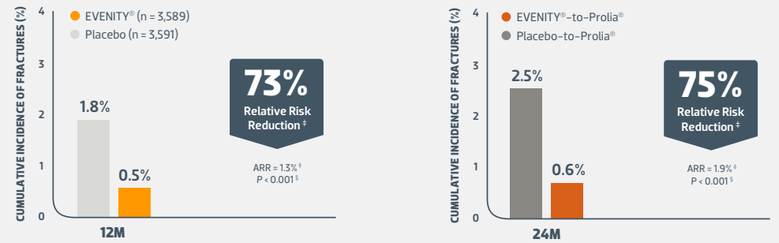
Important Safety Information for Prolia®

Hypocalcemia may worsen with the use of Prolia®, especially in patients with severe renal impairment. Adequately supplement all patients with calcium and vitamin D.

Please see additional Prolia® Important Safety Information on pages 10 and 11.

EVENITY® followed by Prolia® is proven to significantly reduce the risk of new vertebral fractures at 24 months

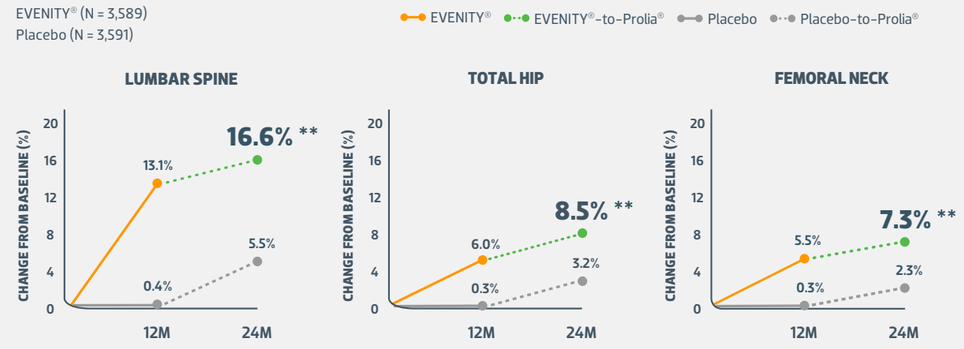
New vertebral fracture risk reduction vs placebo [1]



- The incidence of nonvertebral fractures was not statistically significantly different when comparing EVENITY®-treated women to placebo-treated women at month 12 or month 24 [1]

[‡]Absolute and relative risk reduction are based on the Mantel-Haenszel method adjusting for age and prevalent vertebral fracture strata.
[§]*P* value based on logistic regression model adjusting for age and prevalent vertebral fracture strata.
ARR = absolute risk reduction.

Prolia® continued to improve BMD at multiple sites through 24 months after a strong start with EVENITY® [1,11]



**P < 0.001 based on ANCOVA model adjusting for treatment, age, and prevalent vertebral fracture stratification variables, baseline value, machine type, and baseline value-by-machine type interaction, without adjustment for multiplicity.

Prolia® can help strengthen and protect the bone she's built with EVENITY® [1,12]

Important Safety Information for EVENITY®

Hypocalcemia has occurred in patients receiving EVENITY®. Correct hypocalcemia prior to initiating EVENITY®. Adequately supplement patients with calcium and vitamin D while on EVENITY®.

Please see additional EVENITY® Important Safety Information on page 8.

Plan Prolia® as her next step after EVENITY®

The EVENITY® → Prolia® sequence is a strong choice to help reduce her risk for fracture [1]

Rapidly build bone with 12 monthly doses of EVENITY® [1]

Talk to your patient about transitioning to Prolia® [1]

Transition to Prolia® 1 month * after completion of EVENITY® to improve BMD and reduce vertebral fracture risk at 24 months [1,2]

*In the FRAME study, Prolia® was initiated 1 month +/- 7 days from the last monthly dose of EVENITY®.

AACE guidelines recommend following 12 months of EVENITY® with an antiresorptive treatment like Prolia® [9]

EVENITY® (romosozumab-aqqg) injection 105 mg/1.17 mL | prolia® (denosumab) injection

Important Safety Information for EVENITY®

Hypersensitivity reactions have occurred in EVENITY®-treated patients. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of EVENITY®.

Please see additional EVENITY® Important Safety Information on page 8.

Give your patients 6 months of therapy with each dose of Prolia®

The image above is for illustration purposes only and represents a snapshot in time. Actual dosing and duration of a particular patient's therapy should be based upon the product's approved labeling and the independent clinical decision of the provider.

Prolia® is one shot every 6 months [12]

- 60 mg subcutaneous injection in the upper arm, upper thigh, or abdomen by a healthcare professional
  - Pre-existing hypocalcemia must be corrected prior to initiating therapy with Prolia®
  - Adequately supplement all patients with calcium and vitamin D
  - Multiple vertebral fractures have been reported following Prolia® discontinuation

Important Safety Information for Prolia®

Following discontinuation of Prolia® treatment, fracture risk increases, including the risk of multiple vertebral fractures. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Please see additional Prolia® Important Safety Information on pages 10 and 11.

INDICATION

EVENITY® is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

The anabolic effect of EVENITY® wanes after 12 monthly doses of therapy. Therefore, the duration of EVENITY® use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an antiresorptive agent should be considered.

IMPORTANT SAFETY INFORMATION

POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH

EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY® should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENITY® should be discontinued.

In a randomized controlled trial in postmenopausal women, there was a higher rate of major adverse cardiac events (MACE), a composite endpoint of cardiovascular death, nonfatal myocardial infarction and nonfatal stroke, in patients treated with EVENITY® compared to those treated with alendronate.

Contraindications: EVENITY® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with EVENITY®. EVENITY® is contraindicated in patients with a history of systemic hypersensitivity to romosozumab or to any component of the product formulation. Reactions have included angioedema, erythema multiforme, and urticaria.

Hypersensitivity: Hypersensitivity reactions, including angioedema, erythema multiforme, dermatitis, rash, and urticaria have occurred in EVENITY®-treated patients. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of EVENITY®.

Hypocalcemia: Hypocalcemia has occurred in patients receiving EVENITY®. Correct hypocalcemia prior to initiating EVENITY®. Monitor patients for signs and symptoms of hypocalcemia, particularly in patients with severe renal impairment or receiving dialysis. Adequately supplement patients with calcium and vitamin D while on EVENITY®.

Osteonecrosis of the Jaw (ONJ): ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving EVENITY®. A routine oral exam should be performed by the prescriber prior to initiation of EVENITY®. Concomitant administration of drugs associated with ONJ (chemotherapy, bisphosphonates, denosumab, angiogenesis inhibitors, and corticosteroids) may increase the risk of developing ONJ. Other risk factors for ONJ include cancer, radiotherapy, poor oral hygiene, pre-existing dental disease or infection, anemia, and coagulopathy.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. In these patients, dental surgery to treat ONJ may exacerbate the condition. Discontinuation of EVENITY® should be considered based on benefit-risk assessment.

Atypical Femoral Fractures: Atypical low-energy or low trauma fractures of the femoral shaft have been reported in patients receiving EVENITY®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated.

During EVENITY® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of EVENITY® therapy should be considered based on benefit-risk assessment.

Adverse Reactions: The most common adverse reactions (≥ 5%) reported with EVENITY® were arthralgia and headache.

EVENITY® is a humanized monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Please click here to see EVENITY® full Prescribing Information, including Medication Guide.

References: 1. EVENITY® (romosozumab-aqqg) prescribing information, Amgen. **2.** Data on file, Amgen; 2013. **3.** National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014. **4.** Kendler DL, Bone HG, Massari F, et al. Bone mineral density gains with a second 12-month course of romosozumab therapy following placebo or denosumab. *Osteoporos Int.* 2019;30:2437-2448. **5.** Medicare.gov. Bone mass measurements. Accessed July 15, 2021. https://www.medicare.gov/coverage/bone-mass-measurements. **6.** Lewiecki EM, Binkley N, Morgan SL, et al. Best practices for dual-energy x-ray absorptiometry measurement and reporting: International Society for Clinical Densitometry guidance. *J Clin Densitom.* 2016;19:127-140. **7.** Centers for Medicare and Medicaid Services. Radiology services and other diagnostic procedures. In: *Medicare Claims Processing Manual.* CMS publication 100-04. Accessed July 15, 2021. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c13.pdf. **8.** Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25:2359-2381. **9.** Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis—2020 Update. *Endocr Pract.* 2020;26(suppl 1):1-46. **10.** Cosman F, Crittenden DB, Adachi JD, et al. Romosozumab treatment in postmenopausal women with osteoporosis. *N Engl J Med.* 2016;375:1532-1543. **11.** Lewiecki EM, Dinavahi RV, Lazaretti-Castro M, et al. One year of romosozumab followed by two years of denosumab maintains fracture risk reductions: results of the FRAME extension study. *J Bone Miner Res.* 2019;34:419-428. **12.** Prolia® (denosumab) prescribing information, Amgen.

EVENITY®
(romosozumab-aqqg)
injection 105 mg/1.17 mL

INDICATION

Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

Contraindications: Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Prolia® is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolia®. Prolia® is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

Same Active Ingredient: Prolia® contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia® should not receive XGEVA®.

Hypersensitivity: Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia®.

Hypocalcemia: Hypocalcemia may worsen with the use of Prolia®, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, including treatment with other calcium-lowering drugs, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia® injection. Concomitant use of calcimimetic drugs may worsen hypocalcemia risk and serum calcium should be closely monitored. Adequately supplement all patients with calcium and vitamin D.

Osteonecrosis of the Jaw (ONJ): ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should be performed by the prescriber prior to initiation of Prolia®. A dental examination with appropriate preventive dentistry is recommended prior to treatment in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g. chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolia®. The risk of ONJ may increase with duration of exposure to Prolia®.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia® should be considered based on individual benefit-risk assessment.

Atypical Femoral Fractures: Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolia®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

During Prolia® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of Prolia® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia® Treatment: Following discontinuation of Prolia® treatment, fracture risk increases, including the risk of multiple vertebral fractures. New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of Prolia®. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia® discontinuation. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Serious Infections: In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia®.

Endocarditis was also reported more frequently in Prolia®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

Dermatologic Adverse Reactions: Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia® compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

Musculoskeletal Pain: Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolia®. Consider discontinuing use if severe symptoms develop.

Suppression of Bone Turnover: Prolia® resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions: The most common adverse reactions (>5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

The overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia® group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Please click here to see Prolia® full Prescribing Information, including Medication Guide.

prolia®
(denosumab) injection

For patients completing 12 monthly doses of EVENITY®

Plan her transition to Prolia®

Don't wait—build on her progress following EVENITY® treatment by transitioning to Prolia®. [1]
If a patient does not continue to another osteoporosis treatment, BMD can decline. [1,4]

- Transition to Prolia® 1 month * following completion of EVENITY® treatment [2]
- EVENITY® followed by Prolia® continued to increase BMD through 24 months [1]
- EVENITY® followed by Prolia® lowered the risk of new vertebral fractures by 75% at 24 months compared to placebo followed by Prolia® [1]

*In the FRAME study, Prolia® was initiated 1 month +/- 7 days from the last monthly dose of EVENITY®.

EVENITY® (romosozumab-aqqg) injection 105 mg/1.17 mL

INDICATION

EVENITY® is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

The anabolic effect of EVENITY® wanes after 12 monthly doses of therapy. Therefore, the duration of EVENITY® use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an antiresorptive agent should be considered.

IMPORTANT SAFETY INFORMATION

POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH

EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY® should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENITY® should be discontinued.

Please see additional EVENITY® Important Safety Information on page 8.

prolia® (denosumab) injection

INDICATION

Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

Prolia® is contraindicated in patients with hypocalcemia, women who are pregnant, and patients with a history of systemic hypersensitivity to any component of the product. Perform pregnancy testing in women of reproductive potential prior to initiating treatment with Prolia®.

Please see additional Prolia® Important Safety Information on pages 10 and 11.

AMGEN®